REMARKS

Status of the Claims

Claims 1-3 and 6 are currently pending in the subject application. By this amendment, Claims 1-3 and 6 have been amended without prejudice or disclaimer and claims 8 and 9 have been added. Thus, upon entry of this amendment, Claims 1-3, 6, 8 and 9 will be pending in the subject application.

Claims 1-3 and 6 have been amended to specify that the process is a dynamic irradiation process as opposed to a static process. Claim 1 also has been amended to specify that the heparin is in solution at a concentration between 2 and 25% w/v. Support for these amendments can be found at page 5, lines 6-10, and at page 4, lines 24-27, respectively.

New claims 8 and 9 specify that the depolymerization process is carried out at a temperature of between 10 and 60 °C and that the solution has a concentration between 4 and 15% w/v, respectively. Support for these amendments can be found at page 5, lines 14-15, and at page 4, lines 26-27. No new matter has been added.

Double Patenting Rejection

Claim 1 stands rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1-2 of U.S. Patent No. 7,091,337. Applicants traverse this rejection in view of amended Claim 1, which recites a dynamic irradiation process comprising exposing said heparin in solution at a concentration between 2 and 25% w/v to UV radiation. Applicants respectfully submit that these process parameters are neither taught nor suggested by the subject matter of Claims 1-2 of US Patent No. 7,091,337. The withdrawal of this rejection is accordingly warranted.

Rejections Under 35 U.S.C. §§102(b)

Claims 1-3 and 6 stand rejected under 35 U.S.C. §102(b) as being anticipated by Balazs et al. (*Radiation Research*, 1959, 11, 149-164). Applicants respectfully traverse this rejection in view of amended Claim 1.

The invention of amended Claim 1 is a dynamic irradiation process for the depolymerization of heparin wherein the depolymerized heparin has a M_w less than or equal to 50% of the original M_w of said heparin prior to depolymerization, said dynamic irradiation process comprising exposing said heparin in solution at a concentration between 2 and 25% w/v to UV radiation having a peak of from 245 nm to 260 nm for a sufficient time to reduce the M_w of the depolymerized heparin by at least 50% as compared with the M_w of said heparin prior to said exposure to UV radiation. The subject application defines "dynamic irradiation process" as a process wherein the solution to be irradiated is circulating as a thin layer in a lamp jacket and then returns to a reservoir where it is preferably thermostated. *See* Appl. 10/555,897 at p. 5, lines 8-10.

In contrast to the process of Claim 1, Balazs fails to teach or suggest a dynamic irradiation process in which a solution to be irradiated is circulating as a thin layer in a lamp jacket and then returns to a reservoir. Instead, Balazs discloses static irradiation in which samples were irradiated in either quartz cells or Teflon containers having silica windows. *See* Balazs at p. 150. FIG. 1 of Balazs, reproduced below, is a diagram of the static irradiation chamber employed in the Balazs experiments.

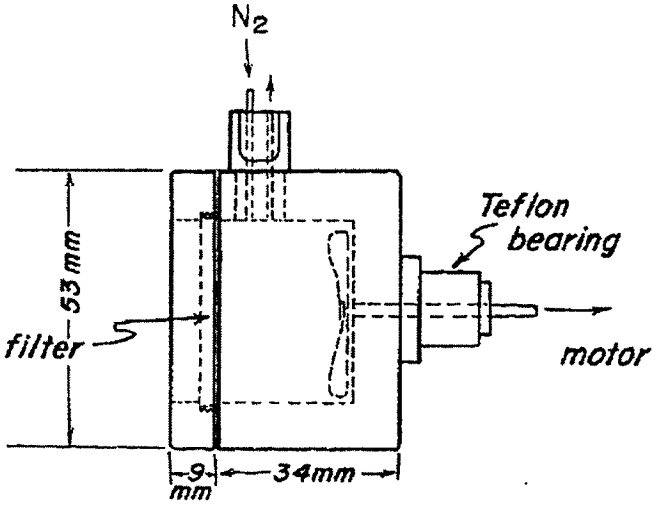

FIG. 1. Diagram of the Teflon radiation chamber

Since Balazs fails to teach a dynamic irradiation process, it cannot anticipate the subject matter of amended Claim 1 or the claims depending therefrom, and the withdrawal of this rejection is respectfully requested.

In addition, Claim 1 of the subject application requires for the heparin to be in solution at a concentration between 2 and 25% w/v. In contrast, the Balazs process operates at much lower concentrations, i.e., concentrations of about 0.1%. *See* Balazs Fig. 2. Applicants assert that Balazs fails to teach or suggest the claimed heparin concentration of Claim 1. For this reason also the withdrawal of the rejection of Claims 1-3 and 6 is respectfully requested.

It should be pointed out that the aforementioned process differences between the presently claimed invention and the Balazs process are significant. For reasons that are not entirely clear, the dynamic irradiation processes of the present invention form compositions having different molecular weight distributions from those formed by the Balazs process. That is, the two processes form different products. *See* De Ambrosi Declaration at ¶ 6.

Balazs reports cationic dyebinding values of dialyzed and undialyzed heparin at time 0, after 120 minutes and after 360 minutes of irradiation. *See* Balazs p. 153, Table 1. Cationic dyebinding is a method to determine the amount of anions present in a molecule. *See* De Ambrosi Declaration at ¶ 8. One characteristic of cationic dyebinding is that the method does not take into account small molecules (e.g., on the order of less than 1,000 Da) that do not precipitate after reaction with the cation. *See id.* at ¶ 9.

Table 1 of Balazs provides lower values for dialyzed heparin than undialized heparain at 120 and 360 minutes after irradiation. These results suggest that the membrane used for dialysis in Balazs removed fragments of heparin that were still capable of precipitating by cationic dyebinding. Those skilled in the art would appreciate that the removed fragments would have a Mw less than 1000 Daltons. *See id.* at ¶ 10. In addition, Table 1 indicates that cationic dyebinding values decreased significantly as irradiation time increased for undialyzed heparin. Specifically, the cationic dyebinding value for undialyzed heparin decreased from 3.90 to 1.59—a reduction of nearly 60%. This pattern suggests that a large amount of very small fragments (less than 1000 Daltons) were formed during the Balazs irradiation process, which fragments did

not precipitate during cationic dyebinding. *See id.* at ¶ 11. The characteristics recited in Table 1 of the Balazs suggest that the Balazs process forms a product having a large fraction of fragments having a Mw less than 1000 Da. *See id.* at ¶ 12.

As indicated in the De Ambrosi Declaration, submitted herewith, the processes of the present invention, in stark contrast to the Balazs processes, form fragments having a Mw less than 1000 Da in an amount less than 6%, even when the overall Mw has been reduced to less than 5000 Da. *See id.* at ¶ 13. Thus, from this information one skilled in the art would expect that cationic dyebinding values of irradiated heparin according to the processes of the present invention would be much higher than those reported in Balazs. *See id.* at ¶ 14. This is a surprising and unexpected result of the process of the present invention, which is strong evidence of the non-obviousness of the presently claimed invention. *See id.* at ¶ 14.

For the foregoing reasons, Applicants respectfully assert that pending Claims 1-3, 6, 8 and 9 are in condition for allowance over the references of record, and a Notice thereof is respectfully requested.

Conclusion

Should the Examiner have any questions regarding this response or the application in general, the Examiner is urged to contact the Applicants' attorney, Justin L. Krieger, by telephone at (202) 625-3858. All correspondence should continue to be directed to the address given below.

Respectfully submitted,

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